



## In re Application of

CHIARELLO et al.

Serial No. 09/921,188

Filed: August 2, 2001

For: PROCESS FOR THE PREPARATION OF CHIRAL ISOFLUOROENES

## Petitions

Art Unit: 1651.

Examiner: Prats, F.C.

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Date of Deposit \_\_\_\_\_

Herbert B. Keil

Person Making Deposit

Signature \_\_\_\_\_

March 6, 2003

Date of Signature

Honorable Commissioner of  
Patents and Trademarks  
Washington, D.C. 20231

PETITION TO THE COMMISSIONER UNDER 37 CFR §1.144

Sir:

Applicants hereby petition the Honorable Commissioner to review the final restriction requirement, dated February 12, 2003.

STATEMENT OF MATERIAL FACTS

1. This application is a US application filed in the US on August 2, 2001, based on the US priority application 60/222,733, which was filed on August 3, 2000.
2. In the first office action dated November 15, 2002, the examiner required restriction pursuant to 35 USC §121, between claims 1-9 (I) and claims 10-11 (II).
3. Applicants filed a timely response to the restriction requirement on December 16, 2002. Applicants elected group I as designated by the examiner with traverse, and reasons for the traversal of the restriction requirement were provided with applicants's response.
4. In a first office action on the merits, dated February 12, 2003 the examiner made the restriction requirement final.
5. Applicants have not yet filed a notice of appeal under 37 CFR §1.191 in this application.

STATUS OF THE CLAIMS

The claims pending in this application are claims 1-10. A copy of the pending claims is found in the attached appendix.

REMARKS

LEGAL STANDARD FOR RESTRICTION

In the Patent Act of 1952, the U.S. Congress created legislation which states, in

pertinent part, that

If two or more independent and distinct inventions are claimed in one application, the Director may require the application to be restricted to one of the inventions.

35 USC §121. Pursuant to its 35 USC §2(b)(2) rulemaking authority, the U.S. Patent and Trademark Office set forward corresponding regulations. These regulations state that

If two or more independent and distinct inventions are claimed in a single application, the examiner in an Office action will require the applicant in the reply to that action to elect an invention to which the claims will be restricted ... .

37 CFR §1.142. The clear intent and meaning of these provisions are that restriction between inventions in a single application is only proper when the pertinent inventions are *both* “independent *and* distinct” (*id*, emphasis added).

Without any supporting documentation, the Manual of Patent Examining Procedure (MPEP) asserts that restriction practice prior to 1952 is sufficient basis to ignore the clear language of the statute and regulation. The MPEP states that

Under the statute an application may properly be required to be restricted to one of two or more claimed inventions only if they are able to support separate patents and they are *either* independent ... *or* distinct ... .

MPEP §803. By replacing the conjunctive article, the MPEP’s authors vastly increased the scope of applications which could be divided. In support of this action, the authors of the MPEP cite a Congressional committee report stating “that [] §121 ‘enacts as law existing practice with respect to division, at the same time introducing a number of

changes.” MPEP §802.01. The argument is made that as the report “does not mention” changes to “the subjects between which the Commissioner may properly require division,” such a change, assertedly, “was clearly not the intent of Congress.” *Id.* This is reasoned despite the plain language of the statute.

However, the intent, or purported lack thereof, of a Congressional committee is not the proper point on which a statute’s interpretation lies, where the statute’s language is clear on its face. Statutory interpretation extends to an examination of legislative intent *only* where the language provided by Congress is vague or prone to misinterpretation. In the present statute, the meaning of the conjunction “and” is straightforward, and needs no interpretive support from the Congressional record. The thin support actually derived from this investigation, and the broad effect it produces on the scope of restriction, only underscore the danger of ignoring the plain meaning of the statute’s language.

According to Congress, the USPTO must demonstrate that inventions in a single application are both independent *and* distinct before restriction is proper. The present examiner has not established that the present claim groupings are *both* independent *and* distinct. Further, the examiner has not demonstrated any legal standard which would support restriction on terms other than those set forward by Congress or by the Commissioner in the statute or regulation. Accordingly, the restriction requirement is legally deficient, and should be withdrawn.

## INDEPENDENCY AND DISTINCTNESS IN THE PRESENT INVENTION

The present claim groupings contain subject matter which is *neither* independent *nor* distinct, and restriction is not proper. Independency, as set forward in the MPEP without reference to case law, occurs when

there is no disclosed relationship between the two or more subjects disclosed, that is, they are unconnected in design, operation, or effect ... .

MPEP §802.01. The present claims 1-9 are directed to certain insecticidal compounds and processes for making these compounds. Present claim 10 is drawn to compounds which are intermediate in the claimed processes. The intermediate compounds are related to the insecticidal compounds as intermediate and product. These claim groupings are therefore not independent, according to the standard set forward above.

Also without reference to case law, the MPEP asserts that distinctness presupposes dependency, and is shown when related subject matter is “capable of separate manufacture, use, or sale as claimed.” MPEP §802.01. In the specific case of intermediate compounds,

Distinctness is proven if it can be shown that the intermediate product is useful other than to make the final product.

MPEP §806.04(b). The original examiner asserted the claimed intermediates to be useful as insecticides, and applicants questioned the sufficiency of this assertion. The present examiner has provided specific examples, alleged to show that intermediates of claim 10 are useful as intermediates.

However, the supplied examples do not, in fact, reflect intermediates as claimed

in claim 10. Rather, these exemplified compounds contain “a group forming insecticidal esters with chrysanthemic acid” at a structural point bearing only hydrogen or methyl groups in the claimed intermediates. Elliott et al. US 4,137,324, abstract. The examiner’s examples do not support the assertion that these intermediates would show comparable insecticidal properties absent the “insecticidal esters.” The presence of such esters teaches away from any insecticidal properties in the present intermediates.

The examiner has not demonstrated that the present intermediates are *both* independent *and* distinct, as required by 35 USC §121 and 37 CFR §1.142. Accordingly, the examiner’s restriction requirement is legally deficient and should be withdrawn.

#### BURDEN ON THE EXAMINER

The restriction requirement should be withdrawn as examination of all present claims will present no serious burden to the examiner. As stated in the MPEP, and yet again without citation,

If the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions.

MPEP §803.01. Further, the examiner asserts, without citation, that

for purposes of the initial restriction requirement a serious burden on the examiner may be *prima facie* shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP §808.02. That *prima facie* showing may be rebutted by appropriate showings or evidence by the

applicant.

Office Action of February 12, 2003, p.2. Applicants see no reference to a *prima facie* showing of a serious burden recited in the cited section, nor do they see a requirement that the applicants rebut this showing “by appropriate showings or evidence.” *Id.* The cited section states that

the examiner, in order to establish reasons for insisting upon restriction, must show by appropriate explanation one of the following: ... .

MPEP §808.02. The examiner shoulders the burden to show “by appropriate explanation” relevant indicators sufficient to “establish reasons for insisting upon restriction.” *Id.*

In the present case, the examiner has not met this burden. Rather than demonstrating “clearly different classifications of the two inventions,” the assertions on this point either bolster the overlapping classification, or obscure the analysis.

Specifically, the original examiner set forward classification in the following manner:

- I. Claims 1-9, drawn to a process for the preparation of a chiral compound, classified in class 435, subclass 132 and a chiral compound classified in class 560, subclass 55+ and class 562, subclass 465.
- II. Claims 10 and 11, drawn to chiral compound, classified in classes 562, 560, 568, and 558, subclass various.

Office Action of November 15, 2002, p.2. Excluding the process claims, all of the present subject matter is to be found in one of four classes, and portions of two of these classes have already been searched. The vague “subclass various” language masks the actual extent to which the two groupings overlap. Applicants submit that the

examiner cannot fairly be said to have shown "by appropriate explanation" separate classification of the above claim groupings sufficient "to establish reasons for insisting upon restriction." MPEP §808.02.

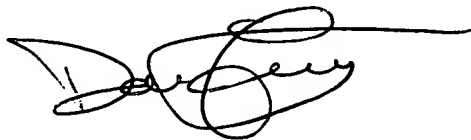
CONCLUSION

In view of the foregoing remarks, it is urged that the examiner's restriction requirement be withdrawn, and that the application be returned to the examiner for further examination.

**A check to cover the petition fee of \$130.00 is attached.**

Please charge any shortage in fees due in connection with the filing of this paper, including Extension of Time fees to Deposit Account No. 11-0345. Please credit any excess fees to such deposit account.

Respectfully submitted,  
KEIL & WEINKAUF

A handwritten signature in black ink, appearing to read "David C. Liechty", with a stylized flourish extending to the right.

David C. Liechty  
Reg. No. 48,692

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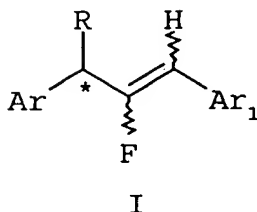
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APPENDIX

PRESENT CLAIMS

1. A process for the preparation of a chiral compound of formula I



wherein

Ar is phenyl optionally substituted with any combination of from one to three halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy, C<sub>1</sub>-C<sub>4</sub>haloalkoxy or hydroxy groups,  
1- or 2-naphthyl optionally substituted with any combination of from one to three halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups, or  
a 5- or 6-membered heteroaromatic ring optionally substituted with any combination of from one to  
three halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups;  
R is C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>3</sub>-C<sub>6</sub>cycloalkyl or C<sub>3</sub>-C<sub>6</sub>halocycloalkyl;  
Ar<sub>1</sub> is phenoxyphenyl optionally substituted with any combination of from one to six halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups,  
phenyl optionally substituted with any combination of from one to five halogen, C<sub>1</sub>-C<sub>4</sub>alkyl,

C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups,

biphenyl optionally substituted with any combination of from one to five halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups,

phenoxy pyridyl optionally substituted with any combination of from one to five halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups,

benzylpyridyl optionally substituted with any combination of from one to five halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups,

benzylphenyl optionally substituted with any combination of from one to five halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups,

benzoylphenyl optionally substituted with any combination of from one to five halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups,

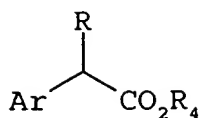
1- or 2-naphthyl optionally substituted with any combination of from one to three halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups, or

a 5- or 6-membered heteroaromatic ring optionally substituted with any combination of from one to three halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups, and

the (E)- and (Z)- isomers thereof,

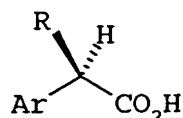
which process comprises the following steps:

a) treating a racemic ester of formula II



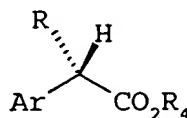
II

wherein Ar and R are defined as hereinabove and R<sub>4</sub> is C<sub>1</sub>-C<sub>4</sub>alkyl with an esterase to form a first mixture of either R-acid IIIa and S-ester IIIb



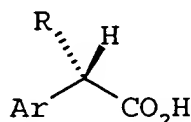
IIIa

and



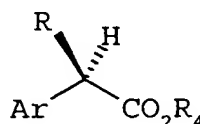
IIIb

or of S-acid IIIc and R-ester IIId



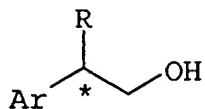
IIIc

and



IIId

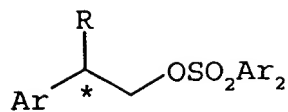
- b) separating said acid IIIa or IIIc from said ester IIIb or IIId;
- c) reducing said acid IIIa or IIIc or said ester IIIb or IIId to obtain a chiral alcohol IV having the R- or S-configuration



IV

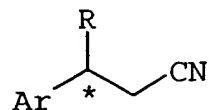
- d) reacting said chiral alcohol with an arylsulfonyl halide Ar<sub>2</sub>SO<sub>2</sub>X

wherein Ar<sub>2</sub> is phenyl, p-chlorophenyl, or p-tolyl, and X is chloro, bromo or fluoro to afford a sulfonate of formula V



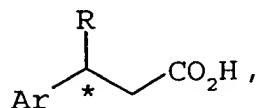
V

e) reacting said sulfonate V with a cyanide-delivering agent to afford a nitrile of formula VI



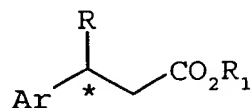
VI

f) hydrolyzing said nitrile VI to afford an acid of formula VII



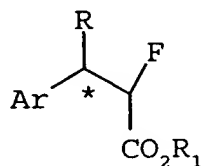
VII

g) esterifying said acid VII with an alcohol  $\text{R}_1\text{OH}$ , wherein  $\text{R}_1$  is  $\text{C}_1$ - $\text{C}_4$  alkyl to afford an ester of formula VIII



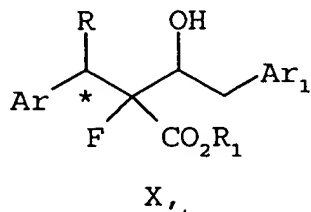
VIII

h) fluorinating said ester to afford a fluoro-ester of formula IX



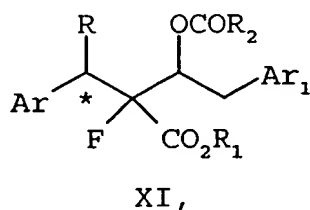
IX

i) reacting said fluoro ester with an aldehyde  $\text{Ar}_1\text{CH}_2\text{CHO}$ , wherein  $\text{Ar}_1$  is defined as hereinabove, in a solvent in the presence of a base to afford a second mixture of 4 chiral diastereomeric hydroxy-esters of formula X;



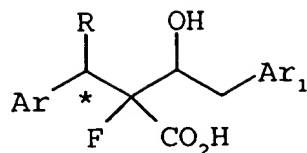
j) optionally separating said second mixture X into a third mixture Xa and a fourth mixture Xb, each mixture having two chiral diastereomers;

k) treating said hydroxy-ester mixture X, Xa or Xb with an acylating agent  $\text{R}_2\text{COX}_1$ , wherein  $\text{R}_2$  is  $\text{C}_1$ - $\text{C}_4$ alkyl and  $\text{X}_1$  is Cl, Br or  $\text{R}_2\text{COO}$ , to afford a fifth mixture of 4 chiral diastereomeric acyloxy esters XI, a sixth mixture of 2 acyloxy esters of formula XIa, or a seventh mixture of 2 chiral diastereomeric acyloxy esters XIb



l) optionally separating said sixth or seventh mixture into essentially pure chiral diastereomeric acyloxy esters;

m) hydrolyzing said pure chiral acyloxy esters or mixtures of esters of formula XI to afford a hydroxy-acid of formula XII,



XII

and

n) heating said hydroxy-acid XII with an arylsulfonyl halide  $\text{Ar}_3\text{SO}_2\text{X}_2$ , wherein  $\text{Ar}_3$  is phenyl, p-chlorophenyl, or p-tolyl, and  $\text{X}_2$  is chloro or bromo to afford the desired chiral compound of formula I.

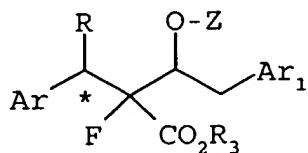
2. The process according to claim 1 wherein said esterase is horse liver esterase.

3. The process according to claim 1 wherein said base is lithium diisopropylamide.

4. The process according to claim 1 wherein said solvent is tetrahydrofuran.

5. The process according to claim 1 wherein  $\text{R}_4$  is methyl.

6. A chiral compound of the following formula



XIII

wherein

Ar is phenyl optionally substituted with any combination of from one to three halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy, C<sub>1</sub>-C<sub>4</sub>haloalkoxy or hydroxy groups,

1- or 2-naphthyl optionally substituted with any combination of from one to three halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups, or

a 5- or 6-membered heteroaromatic ring optionally substituted with any combination of from one to three halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups;

R is C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>3</sub>-C<sub>6</sub>cycloalkyl or C<sub>3</sub>-C<sub>6</sub>halocycloalkyl;

Ar<sub>1</sub> is phenoxyphenyl optionally substituted with any combination of from one to six halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups,

phenyl optionally substituted with any combination of from one to five halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups,

biphenyl optionally substituted with any combination of from one to five halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups,

phenoxyphenyl optionally substituted with any combination of from one to five halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups,

benzylpyridyl optionally substituted with any combination of from one to five halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups,

benzylphenyl optionally substituted with any combination of from one to five halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups,

benzoylphenyl optionally substituted with any combination of from one to five halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups,

1- or 2-naphthyl optionally substituted with any combination of from one to three halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups, or

a 5- or 6-membered heteroaromatic ring optionally substituted with any combination of from one to three halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups, and

R<sub>3</sub> is H or C<sub>1</sub>-C<sub>4</sub> alkyl; and

Z is H or COR<sub>2</sub>, wherein R<sub>2</sub> is C<sub>1</sub>-C<sub>4</sub> alkyl.

7. The compound according to claim 6 wherein Ar is phenyl optionally substituted with any combination of from one to three halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy or C<sub>1</sub>-C<sub>4</sub>haloalkoxy groups; and R is C<sub>1</sub>-C<sub>4</sub>alkyl or C<sub>3</sub>-C<sub>6</sub>cycloalkyl.

8. The compound according to claim 7 wherein Ar<sub>1</sub> is phenyl optionally substituted with one to three halogen groups; and R is C<sub>3</sub>-C<sub>6</sub>cycloalkyl.

9. The compound according to claim 8 selected from the group consisting of



methyl (2S,3S)-2-[(R)-(4-chlorophenyl)(cyclopropyl)-  
methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-  
butanoate;  
methyl (2R,3R)-2-[(R)-(4-chlorophenyl)(cyclopropyl)-  
methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-  
butanoate;  
methyl (2S,3R)-2-[(R)-(4-chlorophenyl)(cyclopropyl)-  
methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-  
butanoate;  
methyl (2R,3S)-2-[(R)-(4-chlorophenyl)(cyclopropyl)-  
methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-  
butanoate;  
methyl (2S,3S)-2-[(S)-(4-chlorophenyl)(cyclopropyl)-  
methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-  
butanoate;  
methyl (2R,3R)-2-[(S)-(4-chlorophenyl)(cyclopropyl)-  
methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-  
butanoate;  
methyl (2S,3R)-2-[(S)-(4-chlorophenyl)(cyclopropyl)-  
methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-  
butanoate;  
methyl (2R,3S)-2-[(S)-(4-chlorophenyl)(cyclopropyl)-  
methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-  
butanoate;  
methyl (2S,3S)-3-(acetyloxy)-2-[(S)-(4-chlorophenyl)-  
(cyclopropyl)methyl]-2-fluoro-4-(4-fluoro-3-  
phenoxyphenyl)butanoate;  
methyl (2R,3R)-3-(acetyloxy)-2-[(S)-(4-chlorophenyl)-  
(cyclopropyl)methyl]-2-fluoro-4-(4-fluoro-3-  
phenoxyphenyl)butanoate;  
methyl (2R,3R)-3-(acetyloxy)-2-[(S)-(4-chlorophenyl)-  
(cyclopropyl)methyl]-2-fluoro-4-(4-fluoro-3-  
phenoxyphenyl)butanoate;

methyl (2S,3R) -3- (acetyloxy) -2- [(S) - (4-chlorophenyl) -  
(cyclopropyl)methyl] -2-fluoro-4- (4-fluoro-3-  
phenoxyphenyl) butanoate;

methyl (2S,3S) -3- (acetyloxy) -2- [(R) - (4-chlorophenyl) -  
(cyclopropyl)methyl] -2-fluoro-4- (4-fluoro-3-  
phenoxyphenyl) butanoate;

methyl (2R,3R) -3- (acetyloxy) -2- [(R) - (4-chlorophenyl) -  
(cyclopropyl)methyl] -2-fluoro-4- (4-fluoro-3-  
phenoxyphenyl) butanoate;

methyl (2R,3S) -3- (acetyloxy) -2- [(R) - (4-chlorophenyl) -  
(cyclopropyl)methyl] -2-fluoro-4- (4-fluoro-3-  
phenoxyphenyl) butanoate;

methyl (2S,3R) -3- (acetyloxy) -2- [(R) - (4-chlorophenyl) -  
(cyclopropyl)methyl] -2-fluoro-4- (4-fluoro-3-  
phenoxyphenyl) butanoate;

(2S,3S) -2- [(S) - (4-chlorophenyl) (cyclopropyl)methyl] -2-  
fluoro-4- (4-fluoro-3-phenoxyphenyl) -3-hydroxy-  
butanoic acid;

(2R,3R) -2- [(S) - (4-chlorophenyl) (cyclopropyl)methyl] -2-  
fluoro-4- (4-fluoro-3-phenoxyphenyl) -3-hydroxy-  
butanoic acid;

(2R,3S) -2- [(S) - (4-chlorophenyl) (cyclopropyl)methyl] -2-  
fluoro-4- (4-fluoro-3-phenoxyphenyl) -3-hydroxy-  
butanoic acid;

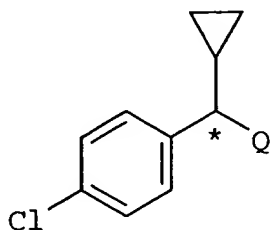
(2S,3R) -2- [(S) - (4-chlorophenyl) (cyclopropyl)methyl] -2-  
fluoro-4- (4-fluoro-3-phenoxyphenyl) -3-hydroxy-  
butanoic acid;

(2S,3S) -2- [(R) - (4-chlorophenyl) (cyclopropyl)methyl] -2-  
fluoro-4- (4-fluoro-3-phenoxyphenyl) -3-hydroxy-  
butanoic acid;

(2R,3R) -2- [(R) - (4-chlorophenyl) (cyclopropyl)methyl] -2-  
fluoro-4- (4-fluoro-3-phenoxyphenyl) -3-hydroxy-  
butanoic acid;

(2R,3S)-2-[(R)-(4-chlorophenyl)(cyclopropyl)methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-3-hydroxybutanoic acid; and  
(2S,3R)-2-[(R)-(4-chlorophenyl)(cyclopropyl)methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-3-hydroxybutanoic acid.

10. A chiral compound of the following formula



wherein

Q is  $-\text{CO}_2\text{H}$ ;  $-\text{CO}_2\text{CH}_3$ ;  $-\text{CH}_2\text{OH}$ ;  $-\text{CH}_2\text{OSO}_2\text{Ar}_2$ ;  $-\text{CH}_2\text{CN}$ ;  $-\text{CH}_2\text{CO}_2\text{H}$ ;  $-\text{CH}_2\text{CO}_2\text{R}_1$ ; or  $-\text{CHFCO}_2\text{R}_1$ ;

$\text{Ar}_2$  is phenyl, p-chlorophenyl or p-tolyl; and

$\text{R}_1$  is  $\text{C}_1$ - $\text{C}_4$ alkyl.

11. The compound according to claim 10 selected from the group consisting of

(2R)-2-(4-chlorophenyl)-2-cyclopropylethyl 4-methylbenzenesulfonate;

(2S)-2-(4-chlorophenyl)-2-cyclopropylethyl 4-methylbenzenesulfonate;

(3R)-3-(4-chlorophenyl)-3-cyclopropylpropanenitrile;

(3S)-3-(4-chlorophenyl)-3-cyclopropylpropanenitrile;

(3R)-3-(4-chlorophenyl)-3-cyclopropylpropanoic acid;

(3S)-3-(4-chlorophenyl)-3-cyclopropylpropanoic acid;

methyl (3R)-3-(4-chlorophenyl)-3-cyclopropylpropanoate;

methyl (3S)-3-(4-chlorophenyl)-3-cyclopropylpropanoate;

methyl (3R)-3-(4-chlorophenyl)-3-cyclopropyl-2-fluoropropanoate; and  
methyl (3S)-3-(4-chlorophenyl)-3-cyclopropyl-2-fluoropropanoate.